PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 913453-58PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/CA2005/000250	International filing date *(day/month/year)* 07 February 2005 (07-02-2005)	Priority date *(day/month/year)* 06 February 2004 (06-02-2004)

International Patent Classification (IPC) or national classification and IPC
IPC: ***C07H 21/00*** (2006.01) , ***C12Q 1/68*** (2006.01) , ***C07H 21/04*** (2006.01)

Applicant
CANADIAN BLOOD SERVICES ET AL

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. [X] *(sent to the applicant and to the International Bureau)* a total of 43 sheets, as follows:

      [X] sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. 1 and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
   1 , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- [X] Box No. I Basis of the report
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [X] Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 December 2005 (06-12-2005)	9 June 2006 (09-06-2006)
Name and mailing address of the IPEA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer Nathalie Chartrand (819) 994-2341

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

[X] the international application in the language in which it was filed

[ ] a translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (Rules 12.3(a) and 23.1(b))

[ ] publication of the international application (Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

[ ] the international application as originally filed/furnished

[X] the description:

[X] pages 1-19, 22-25, 28, 30-36 and 38-49 as originally filed/furnished

[X] pages* 20, 21, 21a, 26, 27, 29, 37 and 50-70 received by this Authority on December 6, 2005

[ ] pages* received by this Authority on

[X] the claims:

[ ] pages as originally filed/furnished

[ ] pages* as amended (together with any statement) under Article 19

[X] pages* 71-76 received by this Authority on December 6, 2005

[ ] pages* received by this Authority on

[X] the drawings:

[ ] pages as originally filed/furnished

[ ] pages* received by this Authority on

[ ] pages* received by this Authority on

[X] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-6 and 8-36	YES
	Claims	7	NO
Inventive step (IS)	Claims	1-6 and 9-36	YES
	Claims	7 and 8	NO
Industrial applicability (IA)	Claims	1-36	YES
	Claims	none	NO

2. Citations and explanations (Rule 70.7)

Reference is made to the documents which were cited in the written opinion of the International Searching Authority, namely:

D1: WO 01/32702 A2 (DRK BLUTSPENDEDIENST BADEN-WUERTTEMBERG GMBH) 10 May, 2001.

D2: WO 00/20634 A1 (NOVA MOLECULAR, INC.) 13 April, 2000.

D3: WO 02/068684 A2 (PYROSEQUENCING AB) 6 September, 2002.

D4: WO 02/30950 A2 (GENAISSANCE PHARMACEUTICALS, INC.) 18 April, 2002

D5: HIRSCHHORN, J. N. et al., "SBE-TAGS: An array-based method for efficient single-nucleotide polymorphism genotyping", Proceedings of the National Academy of Sciences of USA, August 2000, Vol. 97, no. 22, pages 12164-12169.

D6: GRAF, S. et al., "Genotyping of HPA-1 (Human Platelet Antigen 1) by mini-sequencing", Blood. 16 November, 2000, Vol. 96, no. 11, Part 2, page 53b.

D7: GASSNER, C. et al., "RHD/CE typing by polymerase chain reaction using sequence-specific primers", Transfusion. October 1997, Vol. 37, pages 1020-1026.

The point of invention of this application is to provide a multiplex PCR oligonucleotide extension assay to genotype a plurality of blood group or platelet antigen SNPs simultaneously.

NOVELTY AND INVENTIVE STEP under Articles 33(2) and 33(3):

D1 discloses methods to genotype RHD alleles. These methods simultaneously analyze a plurality of polymorphisms (see page 57) which comprise a step of multiplexing PCR amplification. Also, this reference discloses PCR primers used in the methods. The teaching of this reference falls within the scope of claim 7. Therefore, this claim does not comply with Article 33(2) of the PCT. In the correspondence dated December 6, 2005, the applicant argues that the teaching of D1 is different from the present application because it is restricted to a PCR methodology and primers having specificity to a single SNP of only one blood group antigen, that being RhD. However, it appears from page 57, that they analyze more than one SNP of RhD. Claim 7 does not specify that the oligonucleotide primers and probes are used to analyze a plurality of SNPs corresponding to a plurality of blood group or platelet antigen genotypes simultaneously. Therefore, the subject matter of claim 7 is encompassed by D1.

As claim 7 has been found to lack novelty under Article 33(2) of the PCT, it also lacks an inventive step under Article 33(3) of the PCT.

D3 discloses methods of allele-specific primer extension useful for detecting mutations and genetic variations. Human genomic DNA is isolated, then, multiplex PCR is performed to amplify multiple single nucleotide polymorphisms. The SNPs analyzed were wiaf1764 (A/C) on chromosome 9q, codon 72 (C/G) on the p53 gene, nucleotide position 677 (C/T) on the MTHFR gene and nucleotide position 196 (A/G) on the GPIIIa gene.

See supplemental sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 9 is ambiguous and does not comply with Article 6 of the PCT. The preliminary paragraph of the claim defines a method of simultaneously analyzing a plurality of blood group or platelet antigens in a sample and in step b), the multiplex PCR amplification of DNA encompasses a plurality of SNPs each corresponding to a blood group or platelet antigen genotype. It is not clear in step b) and according to the first paragraph, whether the SNPs correspond to a plurality of blood group or platelet antigens or to a single blood group or platelet antigen.

In claim 8, the expression "more than one of all of said probe" should be replaced by "more than one or all of the said probe".

Claim 20 is indefinite and does not comply with Article 6 of the PCT. Applicant is claiming a method without fully defining it in the claim. A method is a series of steps to be followed to achieve a desired result. All of the essential steps of the allegedly novel method must be defined.

A typographic error was found in claim 20. The word "the" is repeated in the expression "more of the the oligonucleotide" .

Claim 23 is indefinite and does not comply with Article 6 of the PCT. The "sample" in step (a) has no antecedent.

Supplemental Box relating to Sequence Listing

Continuation of Box No.1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

      [X] a sequence listing

      [X] table(s) related to the sequence listing

   b. format of material

      [X] on paper

      [X] in electronic form

   c. time of filing/furnishing

      [X] contained in the international application as filed

      [ ] filed together with the international application in electronic form

      [ ] furnished subsequently to this Authority for the purposes of search and/or examination

      [X] received by this Authority as an amendment* on December 6, 2005

2. [X] In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V

It is obvious to a skilled person, in view of D3 and common general knowledge, to prepare other primers directed to other blood group antigens in the method to identify blood group SNPs as taught in D3. Therefore, claims 7 and 8 do not define an inventive step under Article 33(3) of the PCT. As mentioned previously, claim 7, on which claim 8 depends, does not specify that the oligonucleotide primers and probes are used to analyze a plurality of SNPs corresponding to a plurality of blood group or platelet antigen genotypes simultaneously. Thus, claims 7 and 8 are not inventive.

The amended claims 1 to 6 and 8 to 36 submitted on December 6, 2005 appear to be novel in view of the cited documents (D1 to D7). More specifically, the applicant has amended claim 1 to specify that the nucleic acid sequences of Table 1 are for use in a PCR primer pair for multiplex SNP analysis of a plurality of blood group or platelet antigen SNPs simultaneously. The examiner agree with the argument outlined by the applicant in the correspondence dated December 6, 2005 which states that neither D1 nor D2 disclose an oligonucleotide primer and probe set for analyzing a plurality of blood group or platelet antigen SNPs simultaneously. Also, some claims (9, 10, 28, 29, 32 and 40) that were rejected for lack of novelty in the Written Opinion of the International Searching Authority have been deleted with the amendments submitted on December 6, 2005, thereby obviating the objection. The new claims 9, 23 and 32 now specify that the methods encompass the simultaneous analysis of a plurality of blood group or platelet antigen specific SNPs and in addition for claims 23 and 32 include the use of a plurality of primers as defined in Table 1.

Also, claims 1 to 6 and 9 to 36 appear to be inventive. The primers of claim 1 are used in a multiplex PCR method for the analysis of a plurality of blood group or platelet antigen SNPs simultanesously. Also, the method claimed in claims 9, 20, 23, 32 and the use claim 26 involve the analysis of more than one blood group or platelet antigen SNPs simultaneously. The teachings of the cited references do not describe nor suggest a methodology or primers for use therein for the simultaneous detection of unrelated blood group and platelet genotypes simultaneously. Therefore, the subject matter defined in those claims is novel and inventive.

INDUSTRIAL APPLICABILITY:

Claims 1 to 36 appear to have industrial applicability under Article 33(4) of the PCT, based on the use of the primers and probes of Tables 1 and 2 in a method of simultaneously analyzing a plurality of blood group or HPA antigens in a sample.